

## REMARKS

Entry of the foregoing, reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

### I. Claim Amendments

By the foregoing amendment, claims 4, 8, 10-14, 16, 17, 19, 23, and 26 have been amended, new claim 38 has been added, and claims 1-3, 5-7, 20-22, 24, and 25 have been canceled.

In particular, claim 19 has been amended to recite that the recombinant virus is an adenovirus, as supported at least by original claims 2 and 3.

The claims have also been amended such that claims 4, 8-19, 23, and 26 all depend ultimately from claim 19 rather than from claim 1.

Claim 17 has been amended to recite that the recombinant adenovirus or a fragment thereof is administered via intravenous injection.

Claim 26 has been amended to recite that the amount of the recombinant adenovirus or a fragment thereof able to form plaques is equal to or greater than about  $8 \times 10^9$  pfu/mouse, as supported at least at page 14, paragraph 46, of the specification, and by the examples shown on page 34 and page 37.

New claim 38 is directed to phenotypic analysis, and recites that "administration of the recombinant adenovirus or a fragment thereof to the mammal causes a specific phenotypic result in the mammal; and [that] the specific phenotypic result is measured by molecular assays and/or clinical markers." Support for claim 38 can be found at least at page 28, paragraph 85, of the specification.

In addition, other amendments to the claims have been made to clarify the claim language and bring the claims into better conformance with U.S. patent practice. These amendments are merely editorial in nature and are not intended to change the scope of the claims or any elements recited therein.

The amendments to the claims, including cancellation of claims, have been made without prejudice or disclaimer to any subject matter recited or canceled herein. Applicants reserve the right to file one or more continuation and/or divisional applications directed to

any canceled subject matter. No new matter has been added, and entry of the foregoing amendments of the above-identified application is respectfully requested.

**II. Response to Claim Rejections Under 35 U.S.C. § 112, Second Paragraph**

At page 4-6 of the Office Action, claims 4, 11 and 19-26 have been rejected under 35 U.S.C. § 112, second paragraph, as purportedly indefinite for the following reasons:

**A.** The Examiner has stated that claim 4 is indefinite for reciting a "fragment" of an adenovirus, because a adenoviral fragments are not encompassed by claim 1 upon which claim 4 depends.

In response, Applicant has amended claim 1 to recite "a virus or a fragment thereof." Applicant notes that corresponding amendments have also been made to the other pending claims as well as to claim 1.

**B.** The Examiner has stated that claim 11 is indefinite for reciting an "additional nucleic acid sequence" that can be "the same as or different" than the nucleic acid sequence recited in claim 1, because it is not clear how the additional nucleic acid sequence can be different from the nucleic acid sequence of claim 1.

In response, claim 11 has been amended by deleting the term "the same as or different."

**C.** The Examiner has stated that claims 19-26 are indefinite for "optionally" administering a virus that does not express the heterologous protein.

Claim 19 has been amended by deleting the "optional" phrase.

In view of the above, Applicant respectfully requests reconsideration and withdrawal of the indefiniteness rejections.

**III. Response to Claim Rejections Under 35 U.S.C. § 112, Second Paragraph**

At pages 6-11 of the Office Action, claims 1-26 have been rejected under 35 U.S.C. § 112, first paragraph, as purportedly lacking enablement.

Specifically, the Examiner has stated that the specification fails to provide an enabling disclosure for inhibiting the formation of neutralizing antibodies against a cytokine by administering an adenovirus prior to or simultaneously with a sequence encoding the cytokine. According to the Examiner, the examples provided in the present specification show that there is no specific dose of recombinant adenovirus that is always "tolerizing"

rather than "immunizing," thus demonstrating the unpredictability in determining a "tolerizing dose." This rejection is respectfully traversed.

Initially, Applicants note that to expedite prosecution in the present application, and not to acquiesce to the Examiner's rejection, the claims have been amended as described above. In particular, claim 19 has been amended to recite that the recombinant virus is an adenovirus, and the dependent claims have been amended to depend ultimately from claim 19. Applicant submits that a person of ordinary skill would have reasonably expected that the claimed methods would be effective in inhibiting formation of neutralizing antibodies directed against a heterologous protein, and that a person of ordinary skill in the art would have been able to determine a "tolerizing" dose without undue experimentation. In particular, as noted in the Declaration of Dr. Amine Abina, submitted herewith, the specification provides exemplary dosages for depleting or inhibiting at least some antigen presenting cells, and also provides a test for determining an effective "tolerizing" dose of recombinant adenovirus or a fragment thereof. (A copy of Dr. Abina's curriculum vitae is also enclosed for the Examiner's reference.)

Thus, the enablement requirement is met for the entire scope of the claims. Accordingly, Applicant respectfully requests reconsideration and withdrawal of this rejection.

**CONCLUSION**

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

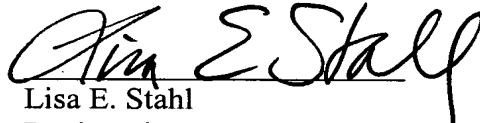
In the event that there are any questions relating to this Reply or the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney so that prosecution of this application may be expedited.

Respectfully submitted,

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